UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF PREVENTION, PESTICIDES AND TOXIC SUBSTANCES

29/DEC/2006

MEMORANDUM

Subject:	EPA File Symbol: #5481-505 **Technical Bifenthrin Insecticide/Miticide**
DP Barcode:	330177
Decision No:	368368
PC Code:	128825
From:	Masih Hashim, Toxicologist Technical Review Branch Registration Division (7505C)
To:	Bewanda Alexander, RM Team 13 Insecticide Branch Registration Division
Applicant:	AMVAC Chemical Corporation Los Angeles, CA 90023

Grant T. Boden 1-3-2007

FORMULATION FROM LABEL:

Active Ingredient(s):	% by wt.
Bifenthrin Technical	96.2
Impurities/ inert ingredients	3.8
Total:	100.0

ACTION REQUIRED: The Risk Manager requested a review of the acute toxicity data for Technical Bifenthrin Insecticide/Miticide (EPA Reg. No. #5481-505).

#5481-505 Bifenthrin
P.C. Code 128825

BACKGROUND: The product is Bifenthrin Insecticide/miticide (96.2%) from AMVAC Chemical Corporation. Registrant submitted new studies on the formulation to revise tox categories (if necessary). Originally it was registered as a similarity product.

Due to the physical nature of the formulation (crystalline or waxy solid on room temperature), the inhalation study is not required.

RECOMMENDATIONS: Each of the five studies (MRID 46821101-05) is in compliance with the Sub-Division F guidelines. The toxicology profile for #5481-505 is as follows:
and is described in the following Table.

acute oral toxicity	II	acceptable	MRID 46821105
acute dermal toxicity	III	acceptable	MRID 46821104
acute inhalation study	-	waived	
primary eye irritation	III	acceptable	MRID 46821102
primary dermal irritation	IV	acceptable	MRID 46821101
dermal sensitization	neg.	acceptable	MRID 46821103

LABELING:

PRODUCT ID #: 005481-00505

PRODUCT NAME: Technical Bifenthrin Insecticide/Miticide

PRECAUTIONARY STATEMENTS
SIGNAL WORD: WARNING

SPANISH SIGNAL WORD:
AVISO

Si usted no entiende la etiqueta, busque a alguien para que se la explique a usted en detalle.
(If you do not understand the label, find someone to explain it to you in detail.)

Hazards to Humans and Domestic Animals:

May be fatal if swallowed. Harmful if absorbed through skin. Causes moderate eye irritation. Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum, or using tobacco. Avoid contact with skin, eyes or clothing. Wear long-sleeved shirt and long pants, socks, shoes, and gloves. Remove and wash contaminated clothing before reuse. Avoid contact with eyes or clothing. Wear protective eyewear.

First Aid:

If swallowed:
-Call a poison control center or doctor immediately for treatment advice.
-Have person sip a glass of water if able to swallow.
-Do not induce vomiting unless told to by a poison control center or doctor.
-Do not give anything to an unconscious person.

If on skin:
-Take off contaminated clothing.
-Rinse skin immediately with plenty of water for 15-20 minutes.
-Call a poison control center or doctor for treatment advice.

If in eyes:
-Hold eye open and rinse slowly and gently with water for 15-20 minutes.
-Remove contact lenses, if present, after the first 5 minutes, then continue rinsing.
-Call a poison control center or doctor for treatment advice.

NOTE TO PHYSICIAN: Note to PM/CRM/Registrant: The proposed label should contain a "Note to Physician". The following statements are suggested types of information that may be included, if applicable: - technical information on symptomatology; - use of supportive treatments to maintain life functions; - medicine that will counteract the specific physiological effects of the pesticide; - company telephone number to specific medical personnel who can provide specialized medical advice.

Have the product container or label with you when calling a poison control center or doctor or going for treatment. You may also contact 1-800-xxx-xxxx for emergency medical treatment information.

Reviewer: Masih Hashim December 29, 2006

Risk Manager (EPA): 13

TYPE OF STUDY : Acute Oral Study in Rats; OPPTS 870.1100; OECD 425

TEST MATERIAL : Bifenthrin Technical Insecticide/Miticide (96.2%), Viscous liquid, crystalline or waxy solid @room temperature.

CITATION : Kuhn, J. (2004). Acute Oral Toxicity Study (UDP) in Rats- Stillmeadow, Inc. Sugar Land, TX 77478. Study No. 8060-04 dated 4-1-04. MRID 46821105. Unpublished.

SPONSOR : Amvac Chemical Corporation, Los Angeles, CA 90023.

EXECUTIVE SUMMARY : In an acute oral toxicity-Up and Down Procedure was used to determine the LD_{50} of Bifenthrin Technical (MRID 46821105). The vehicle used was 2% CMC w/v. The test substance was administered to SD rats (wt. 167-202g females, source: Texas Animal Specialties, Humble, TX). One animal was initially dosed at 5000 mg/kg. The animal died. Additional animals were dosed at 55, 175 and 550 mg/kg in accordance with UDP. Evaluation parameters included signs of gross toxicity and mortality for a subsequent period of 14 days. Initial and weekly body weights, and necropsy findings were recorded on all animals.

Oral LD_{50} for Female rats was 175 mg/kg

Several animals died on the study (Table 1). Decrease in activity, body tremors and convulsions were noted in the rats that died on test. Clinical signs in survivors included crusted nose, diarrhea, piloerection and sensitivity to sound (for a day). Necropsy of decedents showed stained / crusted fur, discolored lungs, liver and contents of g.i tract. There was either gas in stomach or empty g.i tract. Surviving animals showed no lesions.

Based on the LD_{50} the test substance is in Category II.

This acute oral study is Acceptable. This study satisfies the guideline requirement for an acute oral study (OPPTS 870.1100) in the rat.

COMPLIANCE : Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

RESULTS and DISCUSSION :

Table 1. (from 425) It is consistent with the laboratory data.

AOT425statpgm (Version: 1.0) Test Results and Recommendations
Acute Oral Toxicity (OECD Test Guideline 425) Statistical Program

Date/Time: Wednesday, January 03, 2007, 9:45:33 AM
Data file name: Bifenthrin.data
Last modified: 1/3/2007 9:45:30 AM

Test/Substance: Enter test description.
Test type: Main Test
Limit dose (mg/kg): 5000
Assumed LD50 (mg/kg): Default
Assumed sigma (mg/kg): 0.5

Recommended dose progression: 5000, 1750, 550, 175, 55, 17.5, 5.5, 1.75

DATA:

Test Seq.	Animal ID	Dose (mg/kg)	Short-term Result	Long-term Result
1	282	175	O	O
2	283	550	X	X
3	284	175	X	X
4	285	55	O	O
5	286	175	O	O
6	287	550	X	X

(X = Died, O = Survived)

Dose Recommendation: The main test is complete.

Stopping criteria met: LR criterion.

SUMMARY OF LONG-TERM RESULTS:

Dose	O	X	Total
55	1	0	1
175	2	1	3
550	0	2	2
All Doses	3	3	6

Statistical Estimate based on long term outcomes:

Estimated LD50 = 175 (The one dose with partial response).
95% PL Confidence interval is 42.89 to 1040.

A. Mortality : see Table 1.

B. Clinical observations: Several animals died on the study (Table 1). Clinical signs in survivors included crusty nose, diarrhea, piloerection and sensitivity to sound (for 1-2 days). Decrease in activity body tremors and convulsions were noted in rats that died on test.

C. Gross Necropsy - Necropsy of decedents showed stained / crusted fur, rigid limbs, discolored lungs, liver and contents of g.i tract, gas in stomach and/ or empty intestinal tract. Animals surviving to termination showed no lesions.

D. Reviewer's Conclusion: . The product is in EPA Tox Category II with LD_{50} at 175 mg/kg.

Reviewer: M. Hashim December 29, 2006

Risk Manager (EPA): 13

TYPE OF STUDY : Acute Dermal Toxicity- Rabbit; OPPTS 870-1200; OECD 402.

TEST MATERIAL : Bifenthrin Technical Insecticide / Miticide, Viscous liquid, crystalline or waxy solid at room temperature.

CITATION : Kuhn, J. (2004). Acute Dermal Toxicity Study in Rabbits. Sugar Land, TX 77478. Study No. 7704-03 dated 12-15-03. MRID 46821104. Unpublished.

SPONSOR : Amvac Chemical Corporation, Los Angeles, CA 90023.

EXECUTIVE SUMMARY: An acute dermal toxicity study (MRID 46821104) was performed to assess the dermal LD_{50} of Bifenthrin Technical (96.2%) in NZW rabbits (wt. males 2.1-2.3 kg, females 2.0-2.4kg , source- Nichols Rabbitry, Lumberton, TX). Rabbit, (5/sex) received the test substance (dermally) in corn oil (50:50) v/v concentration at 2020 mg/kg, or 5 females (10:1 corn oil conc.) at 200 mg/kg. The test site was covered by a gauze patch and secured by a non irritating adhesive tape. Animals were observed for mortality, clinical signs, and weekly body weights for 14 days. Terminal necropsy findings were recorded.

Dermal LD_{50} Males >2020 mg/kg
Females > 2020 mg/kg

Two of 5 females died at (the days 3 and 6) 2020 mg/kg dose. Clinical signs were seen as decrease in activity, and body tremors. All surviving animals showed no clinical sign. Four males and 3 females lost weight, and one female failed to gain weight between 0-7 days. Dermal irritation consisting of very slight erythema and edema on Day1was seen at the higher dose. Necropsy findings in the decedents showed oral discharge, discolored lungs and liver, large intestine full of green material, gas in g.i tract and empty stomach and /or small intestine.

This acute dermal study is Acceptable, and it does satisfy the guideline requirements for an acute dermal study in rabbit (OPPTS 870.1200; OECD 402). The product is in EPA Tox Category III for dermal toxicity.

COMPLIANCE : Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

RESULTS and DISCUSSION:

Table 1.

Dose (mg/kg bw)	Mortality/ Number Tested		
	Male	Female	Combined
200 2020	- 0/5	0/5 2/5	- 2 / 10

A. Mortality : Two of 5 females died at the 2020 mg/kg dose.

B. Clinical observations : Clinical signs were seen as decrease in activity, and body tremors. All surviving animals showed no clinical sign. Four males and 3 females lost their weight, and one female failed to gain weight between 0-7 days. Dermal irritation was seen in high dose; very slight erythema and edema on Day 1.

D. Conclusion: The product is in EPA tox category III for dermal toxicity (LD_{50} 2020 mg/kg).

Reviewer: M. Hashim December 29, 2006

Risk Manager (EPA): 13

TYPE OF STUDY: Primary Eye Irritation Study in Rabbits, OPPTS 870-2400; OECD 405

TEST MATERIAL : Bifenthrin Technical Insecticide / Miticide (96.2%), Viscous liquid, crystalline or waxy solid @room temperature.

CITATION : Kuhn, J. (2004). Primary Eye Irritation. Stillmeadow, Inc. Sugar Land, TX 77478. Study No. 7706-3 dated 10-22-03. MRID 46821102. Unpublished.

SPONSOR : Amvac Chemical Corporation, Los Angeles, CA 90023.

EXECUTIVE SUMMARY : In a primary eye irritation study (MRID 46821102), 0.1g of Bifenthrin technical was instilled into one eye (conjunctival sac) in each of the six rabbits (source- Nichols Rabbitry, Lumberton, TX). The other eye served as the control. Animals were then observed for ocular irritation for 72 hours.

The test substance caused ocular irritation in the rabbits including corneal opacity and conjunctival effects.(Table 1). Irritation subsided by day 7.

The product is a moderate irritant to the rabbit eye. The test substance meets EPA Toxicity Category III for eye irritation.

This study is classified as Acceptable. It does satisfy the guideline requirement for a primary eye irritation study (OPPTS 870.2400; OECD 405) in the rabbit.

COMPLIANCE : Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided.

RESULTS AND DISCUSSION :

Table 1. No of Rabbits with Number "positive" / Total number of Rabbits tested

Observations	**1 hr(s)**	**24**	**48**	**72**	**4 days**	**7**
Corneal Opacity	0/6	5/6	4/6	2/6	0/6	0/6
Iritis	0/6	0/6	0/6	0/6	0/6	0/6
Conjunctivitis	1/6	5/6	3/6	2/6	1/6	0/6

A. Observations - (Table 1) The test substance produced ocular irritation corneal opacity and conjunctivitis). Irritation subsided within 7 days.

B. Reviewer's Conclusions: The study is in compliance with the Sub Division F guidelines. The product is in EPA Tox Category III for eye irritation.

Reviewer: M. Hashim

December 29, 2006

Risk Manager (EPA): 13

TYPE OF STUDY : Primary Skin Irritation Study in Rabbits, OPPTS 870-2500; OECD 404.
TEST MATERIAL : Bifenthrin Technical Insecticide / Miticide, Viscous liquid, crystalline or waxy solid @room temperature.

CITATION : Kuhn, J. (2003). Acute Dermal Irritation Study in Rabbits. Stillmeadow, Inc. Sugar Land, TX 77478. Study No. 7707-03 dated 10-22-03. MRID 46821101. Unpublished.

SPONSOR : Amvac Chemical Corporation, Los Angeles, CA 90023.

EXECUTIVE SUMMARY : In a primary dermal irritation study (MRID 46821101), six young adult NZW rabbits (2 males and 4 females, source: Nichols Rabbitry, Limberton, TX) were dermally treated on the back of each animal with 0.5 mL of undiluted Bifenthrin Technical (96.2%). The test substance was placed on the skin and covered with semi permeable dressing for four hours. The test sites were evaluated by Draize method after removal of dressing at 1, 24,48, 72 hours, and 7 and 10 days

Results showed irritation to the rabbit skin (erythema and edema) and subsided by 10^{th} day. The PDII was 1.7.

The test substance is slightly irritating to the rabbit skin. It is in EPA Tox Cat IV for dermal irritation.

This study is classified as Acceptable. It does satisfy the guideline requirement of a Primary Dermal Irritation study (OPPTS 870.2500; OECD 404) in the rabbit.

COMPLIANCE : Signed and dated GLP, Quality Assurance and Data Confidentiality statements were provided.

RESULTS and DISCUSSION :

A. Observations - Results showed mild irritation to the rabbit skin (erythema and edema) which subsided by 10th day. The PDII was 1.7.

B.. Reviewer's Conclusions : The product is in EPA Tox Category IV based on the degree of skin irritation followed by test substance treatment for 4 hours.

Reviewer: M. Hashim December 29, 2006

Risk Manager (EPA): 13

TYPE OF STUDY: Dermal Sensitization (LLNA) in Mice, OPPTS 870.2600; OECD 870-2600

TEST MATERIAL : Bifenthrin Technical Insecticide / Miticide, Viscous liquid, crystalline or waxy solid @room temperature.

CITATION : Kuhn, J. (2003). Skin Sensitization: Local Lymph Node Assay in Mice. Stillmeadow, Inc. Sugar Land, TX 77478. Study No. 7708-03 dated 12-2-03. MRID 46821103. Unpublished.

SPONSOR : Amvac Chemical Corporation, Los Angeles, CA 90023.

EXECUTIVE SUMMARY : A Lymph Node Assay (LLNA) was performed (MRID 46821103) to assess the sensitization potential of Bifenthrin Technical (96.2%) in female mice (strain CBA J, weight 21.1-23.5g, source Harlan Sprague Dawley, Indianapolis, IN). Three test groups of mice were treated with 0.025, 0.05 or 0.1% test substance (using acetone-olive oil vehicle), each mouse received 2.5 µL to the dorsum of each year. Animals were treated daily for 3 days. After 2 days rest period animals were injected with tritiated methyl-thymidine (TMT) in the tail vein. Five hours later the animals were sacrificed and the (draining) auricular lymph nodes were dissected and prepared for cell count. A positive control group (HCA 85%) in the vehicle was run simultaneously.

The test substance produced a Stimulation Index (SI) of < 3 in all test groups. Therefore, the test substance is not a sensitizer. The vehicle control animals showed appropriate results.

COMPLIANCE : The test meets GLP requirements. This study is classified as Acceptable for LLNA study (OPPTS 870.2600) in the mouse.

Deficiency- The positive control showed SI <3. Since it is significantly higher than other groups, TRB will accept it for this study. The SI for the positive control should be >3.

PROCEDURE : A Lymph Node Assay (LLNA) was performed (MRID 46821103) to assess the sensitization potential of Bifenthrin Technical (96.2%) in female mice (strain CBA J, weight 21.1-23.5g, source Harlan Sprague Dawley, Indianapolis, IN). Three test groups of mice were treated with 0.025, 0.05 or 0.1% test substance (using acetone-olive oil vehicle), each mouse received 2.5 µL to the dorsum of each year. Animals were treated daily for 3 days. After 2 days rest period animals were injected with tritiated methyl-thymidine (TMT) in the tail vein. Five hours later the animals were sacrificed and the (draining) auricular lymph nodes were dissected and prepared for cell count. A positive control group was run simultaneously.

Vehicle- acetone-olive oil.

Positive Control - (HCA 85%) in acetone-olive oil.

II. RESULTS and DISCUSSION : -

Table 1. Stimulation Index (SI) of all experimental groups

Animal group	Test substance concentration	Average count /mouse	No. of mice/group	Test/ Vehicle control ratio (SI)
Vehicle	NA	1272	5	NA
Test group I	0.025%	1732	5	1.4
II	0.05%	1809	5	1.4
III	0.1%	2181	5	1.7
Positive control -	HCA 85%	3129	5	2.5

A. Reaction

and duration - There was no sensitization reaction in the test based on SI.

B. Reviewer's Conclusions : The product is not a sensitizer. The positive control should have SI as >3. It is significantly higher than test/control groups, but it is a weak positive control.

Acute Tox One Liner:
Barcode: 330177
P.C. Code: 128825
Date : Dec 29, 2006
TEST MATERIAL : Bifenthrin Technical

Study/ Species/ #/ Lab/ date	MRID #	Results	Tox Cat.
Acute oral toxicity/rat/ Stillmeadow Labs/#8060-01/ 4-1-04	46821105	Oral LD_{50} =175 mg/kg females	II
Acute dermal toxicity/rabbit/ Stillmeadow Labs/#7704-03/12-15-03	46821104	Dermal LD_{50}>2020 mg/kg	III
Primary eye irritation/rabbit/ Stillmeadow Labs/ #7706-03/10-22-03	46821102	Moderate irritant	III
Primary dermal irritation/ rabbit/ Stillmeadow Labs/ #7707-03/ 10-22-03	46821101	Mild irritant	IV
Dermal sensitization (LLNA) /mouse/#7708-0312-2-03	46821103	Not a sensitizer	-

PROCEDURE : A Lymph Node Assay (LLNA) was performed (MRID 46821103) to assess the sensitization potential of Bifenthrin Technical (96.2%) in female mice (strain CBA J, weight 21.1-23.5g, source Harlan Sprague Dawley, Indianapolis, IN). Three test groups of mice were treated with 0.025, 0.05 or 0.1% test substance (using acetone-olive oil vehicle), each mouse received 2.5 µL to the dorsum of each year. Animals were treated daily for 3 days. After 2 days rest period animals were injected with tritiated methyl-thymidine (TMT) in the tail vein. Five hours later the animals were sacrificed and the (draining) auricular lymph nodes were dissected and prepared for cell count. A positive control group was run simultaneously.

Vehicle- acetone-olive oil.

Positive Control - (HCA 85%) in acetone-olive oil.

II. RESULTS and DISCUSSION : -

Table 1. Stimulation Index (SI) of all experimental groups

Animal group	Test substance concentration	Average count /mouse	No. of mice/group	Test/ Vehicle control ratio (SI)
Vehicle	NA	1272	5	NA
Test group I	0.025%	1732	5	1.4
II	0.05%	1809	5	1.4
III	0.1%	2181	5	1.7
Positive control -	HCA 85%	3129	5	2.5

A. Reaction and duration - There was no sensitization reaction in the test based on SI.

B. Reviewer's Conclusions : The product is not a sensitizer. The positive control should have SI as >3. It is significantly higher than test/control groups, but it is a weak positive control.